I. Description

Growth hormone therapy is a long-term, injectable therapy primarily used in children and adolescents with documented growth hormone deficiencies. Human growth hormone (GH), also known as somatotropin, is synthesized in the somatotrophic cells of the pituitary gland. Since 1985, recombinant GH has been marketed as replacement therapy for children and adults with various diagnoses.

II. Criteria/Guidelines

Initial therapy with human growth hormone is covered (subject to Limitations/ Exclusions and Administrative Guidelines) for one of the following indications:

A. Children with evidence of growth hormone deficiency (GHD) must meet the following criteria:
   1. Biochemical Criteria:
      a. Documentation of abnormal responses to two growth hormone (GH) stimulation tests defined as less than 10 nanograms per milliliter (ng/mL) or as otherwise determined by the testing lab; or
      b. At least one GH stimulation test response less than 15 ng/ml, and both IGF-I and IGF-BP3 levels below normal for age and gender; or
      c. One GH stimulation test response below 10 ng/ml with defined CNS pathology, history of cranial irradiation or genetic conditions associated with GHD; or
      d. Two or more documented pituitary hormone deficiencies other than GH; or
      e. Abnormally low GH level documented in association with neonatal hypoglycemia; and
   2. Auxologic Criteria
      a. Height equal to or less than two standard deviations below the mean for age and gender; or
      b. Height equal to or less than one standard deviation below the mean and growth velocity less than one standard deviation below the mean for age and gender; and
         i. A minimum of one year of growth data is required with measurements at least six months apart and performed by an endocrinologist; or
ii. Patient must have four or more height determinations measured at least six months apart, by the patient’s primary care physician, over a period of at least two years. Results must show a consistent growth pattern; and

c. Radiologic documentation of open growth plates in patients over 12 years of age.

B. Children with idiopathic short stature, familial short stature, or small for gestational age infants with failure of catch-up growth by the age of two must meet the following criteria:
   1. Auxologic Criteria:
      a. Height less than or equal to 2.25 standard deviations below the mean for age and gender; and
      b. Growth velocity equal to or less than one standard deviation below the mean for age and gender measured in accordance with II.A.2.b; and
      c. Radiologic documentation of open growth plates in patients over 12 years of age.

C. Turner’s syndrome: Patients must meet the following criteria:
   1. Open growth plates in patients over 12 years of age; and
   2. Height below the tenth percentile for age.

D. Noonan’s syndrome: Patients must meet the following criteria:
   1. Open growth plates in patients over 12 years of age; and
   2. Height below the tenth percentile for age and gender.

E. Prader-Willi syndrome: Patients must meet the following criteria:
   1. Open growth plates in patients over 12 years of age; and
   2. Height below the tenth percentile for age and gender.

F. Children with chronic renal insufficiency: Patients must meet the following criteria:
   1. Creatinine clearance less than or equal to 75 mL/min per 1.73 m² or serum creatinine greater than 3.0 mg/dl, or dialysis dependent; and
   2. Radiographic documentation of open growth plates in patients over 12 years of age; and

G. Acquired Immune Deficiency Syndrome (AIDS) wasting: Patients must meet the following criteria:
   1. Greater than 10 percent of baseline weight loss that cannot be explained by a concurrent illness other than HIV infection; and
   2. Simultaneous treatment with antiviral agents.

H. Burn patients: Patients must meet the following criteria:
   1. Extensive 3rd-degree burns; or
   2. Burns greater than or equal to 40 percent total body surface area.

I. Short bowel syndrome: Patients must meet the following criteria:
   1. Receiving specialized nutritional support; and
   2. Optimal management of short bowel syndrome.
J. **Adults with evidence of GH deficiency**

1. Irreversible hypothalamic/pituitary structural lesions or ablation: no further testing needed.
2. Defect in GH synthesis: no further testing needed.
3. GH deficiency in childhood, circumstances other than J.1 or J.2. Only about 25% of children with GH deficiency will be found to have GH deficiency as adults. Therefore, once adult height has been achieved, patients should be retested for GH deficiency after at least a one month break in GH therapy to determine if continuing replacement is necessary in accordance with one of the following criteria:
   a. Three or more pituitary hormone deficiencies and IGF-1 level below laboratory’s range of normal: no further testing necessary;
   b. Peak GH level in response to insulin tolerance test less than or equal to 5.0 ng/ml and IGF-1 level below laboratory’s range of normal;
   c. Peak GH level in response to glucagon stimulation test less than or equal to 3.0 ng/ml and IGF-1 level below laboratory’s range of normal;
   d. Peak GH level in response to arginine stimulation test less than or equal to 0.4 ng/ml and IGF-1 level below laboratory’s range of normal.

Note: Levodopa and clonidine stimulation tests are not acceptable for documenting persistence of GH deficiency into adulthood.

Continuation of therapy is covered (subject to Limitations/Exclusions and Administrative Guidelines) when the continuation of therapy criteria listed in the chart below (in Administrative Guidelines) are met.

III. **Administrative Guidelines**

A. Precertification is required. To precertify, please complete HMSA’s Precertification Request and mail or fax the form as indicated.
B. Children approved for GHT under previous HMSA policies will be approved for continuation of therapy in accordance with current continuation criteria.
C. Children receiving GHT without previous HMSA authorization will be considered for continuation of therapy in accordance with current initiation criteria (per clinical data prior to initiation of therapy) and current continuation criteria (per current clinical data).
D. Children previously treated with GHT but who have had treatment subsequently discontinued will be considered for re-initiation of therapy in accordance with current initial treatment criteria (per current clinical data) and continuation criteria except growth velocity (per current clinical data).
## Table 1

<table>
<thead>
<tr>
<th>Indication</th>
<th>Initial Authorization Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric short stature</td>
<td>Up to 12 months</td>
</tr>
<tr>
<td>Turner’s syndrome</td>
<td></td>
</tr>
<tr>
<td>Noonan’s syndrome</td>
<td></td>
</tr>
<tr>
<td>Prader-Willi syndrome</td>
<td></td>
</tr>
<tr>
<td>Chronic Renal Insufficiency</td>
<td></td>
</tr>
<tr>
<td>Adult GHD</td>
<td></td>
</tr>
<tr>
<td>Burn patients</td>
<td>Up to 12 months</td>
</tr>
<tr>
<td>Short bowel syndrome</td>
<td>Four weeks</td>
</tr>
<tr>
<td>AIDS wasting</td>
<td>Up to 12 months</td>
</tr>
</tbody>
</table>

## Table 2

<table>
<thead>
<tr>
<th>Indication</th>
<th>Continuation of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth hormone deficiency</td>
<td>Approved in 12 month increments with current documentation of:</td>
</tr>
<tr>
<td>Pediatric short stature</td>
<td>• Growth velocity greater than or equal to two centimeters per year; and</td>
</tr>
<tr>
<td>Turner’s syndrome</td>
<td>• Open growth plates in children over 12 years of age; and</td>
</tr>
<tr>
<td>Noonan’s syndrome</td>
<td>• Height less than fifth percentile of normal adult height for gender (150 centimeters for girls, 165 centimeters for boys).</td>
</tr>
<tr>
<td>Prader-Willi syndrome</td>
<td></td>
</tr>
<tr>
<td>Chronic Renal Insufficiency</td>
<td></td>
</tr>
<tr>
<td>Adult GHD</td>
<td>Can be approved in 12 month increments</td>
</tr>
<tr>
<td>Short bowel syndrome</td>
<td>No further authorization shall be given</td>
</tr>
<tr>
<td>Burn patients</td>
<td></td>
</tr>
<tr>
<td>AIDS wasting</td>
<td></td>
</tr>
</tbody>
</table>

### Codes

<table>
<thead>
<tr>
<th>Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J2941 and NDC number</td>
<td>Injection somatropin, 1 mg (e.g. Nutropin/Nutropin AQ)</td>
</tr>
</tbody>
</table>
IV. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

V. References

3. Consensus Guidelines for the Diagnosis and Treatment of Adults with Growth Hormone Deficiency: Summary Statement of the Growth Hormone Research Society Workshop on Adult Growth Hormone
8. Genentech product information, Nutropin/Nutropin AQ, April 2012.

VI. Appendix

The values corresponding to specific z-scores are contained in this Excel data file. This file contains the z-scores values for gender (1=male; 2=female). For example, 1.5 months represents 1.25-1.75 months. The only exception is birth, which represents the point at birth.

*Centers for Disease Control and Prevention Growth Chart*

*Z-Score Data Files*